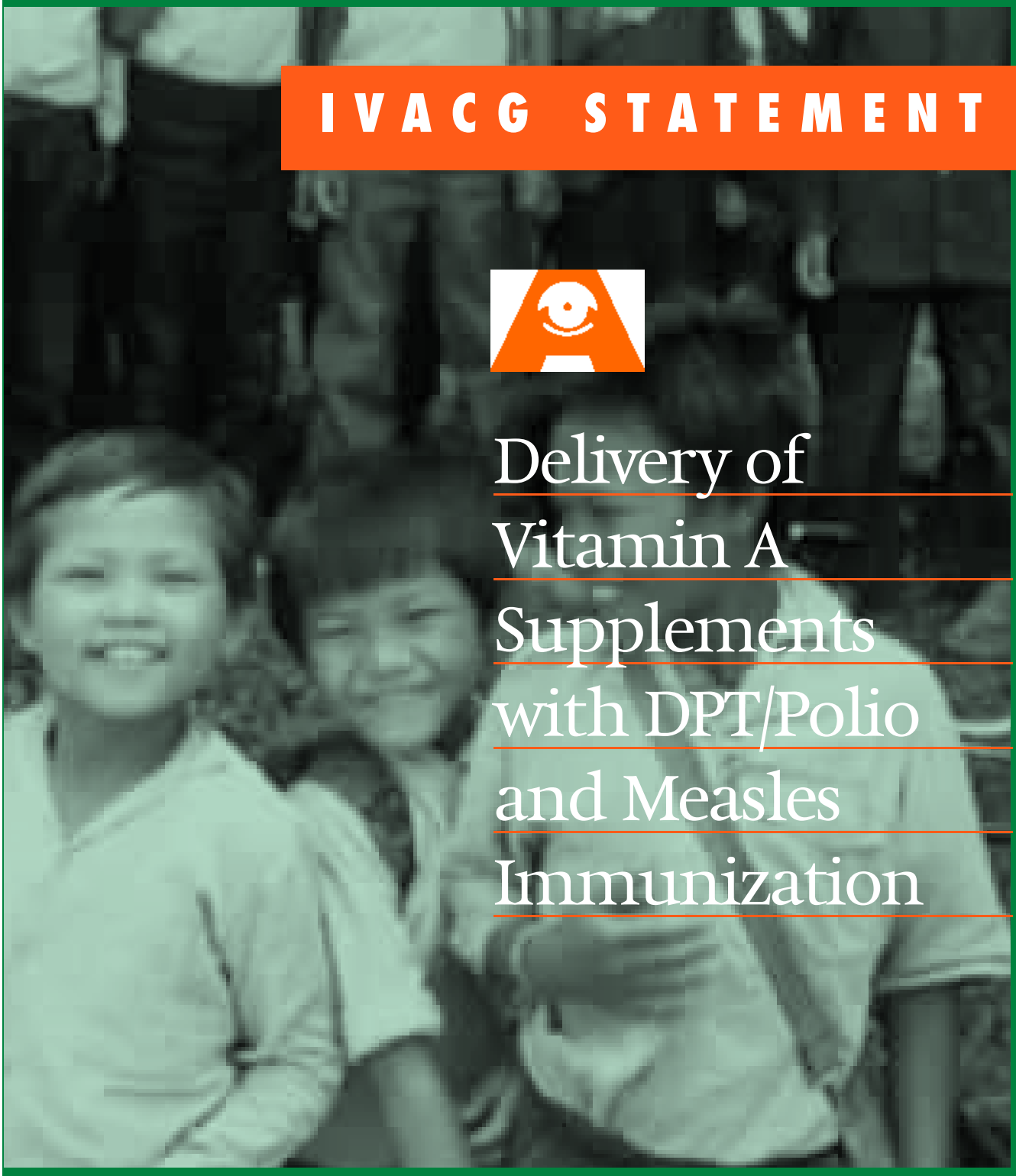
IVACG STATEMENT



Delivery of Vitamin A Supplements with DPT/Polio and Measles Immunization

International Vitamin A Consultative Group

AUGUST 2000

Data accumulated from large field trials over the past fifteen years show conclusively that improving the vitamin A status of children, in areas where vitamin A deficiency is endemic, significantly reduces their risk of severe morbidity (Arthur et al., 1992; Barreto et al., 1994; Biswas et al., 1994) and mortality (Beaton et al., 1993; Fawzi et al., 1993; Glaziou and Mackerras, 1993; Tonascia 1993). Vitamin A supplementation is therefore included in child survival programs in many countries, and it is being recommended for delivery to children at the time that they receive their basic immunizations (WHO, 1994). Three principal strategies have been identified for improving the vitamin A status of populations: supplementation of high risk groups; food fortification; and increasing the production and consumption of locally available vitamin A-rich foods. Although originally regarded as a short- to medium-term strategy, supplementation may, in some situations, offer the most feasible and cost effective means for the control of vitamin A deficiency, even in the long term. The current policy for supplementation of infants recommends a first delivery of 100,000 IU of vitamin A at the earliest opportunity after six months of age, and subsequently at four to six monthly intervals (WHO, 1997).

In most national programs, children receive their first dose of supplements at the time of their measles immunization (usually after nine months of age). Similar opportunities for delivery of supplements to even younger infants (less than six months of age) occur at the time of their diphtheria, pertussis, tetanus (DPT) immunizations within the Expanded Programme on Immunization (EPI), which is known to reach a significant percentage of young infants even in low income countries. To take advantage of these earlier infant contacts with the health service, a schedule for infant vitamin A supplementation was proposed to provide 25,000 IU of vitamin A with each of the DPT/polio immunizations (WHO, 1993). Although there is currently no evidence of similar morbidity and mortality benefits to supplementation of young infants, the expectation was that this would improve the vitamin A status of infants at six months of age, and possibly up to nine months of age.

The safety of vitamin A supplementation to infants at six months of age or older has been established. However, there are two key issues relating to young infants that need to be addressed: the first is the size and safety of the supplemental dose; and the second concerns possible negative impacts on the effectiveness of DPT and polio immunizations when given concurrently with vitamin A. Delivery of vitamin A supplements with DPT/polio immunizations is now occurring in at least one national program (Bangladesh) and has been found to be well-tolerated by young infants. While a higher incidence of bulging of the anterior fontanel has been reported with this regimen (de Francisco et al., 1993), the bulging has been found to be benign, that is, without clinical evidence that it increased intra-cranial pressure or intra-cranial pathology. Also, it is transient, disappearing within 48 hours, and having no long-term developmental sequelae.

The regimen of dosing a young infant, combined with a large dose supplement to the mother in the immediate post-partum period, was recently evaluated in a WHO coordinated multicenter trial (in Ghana, India, and Peru—WHO/CHD Immunisation-Linked Vitamin A Supplementation Multicentre Group, 1998). The results show that adding vitamin A supplementation to DPT/polio

This statement was prepared at the request of the International Vitamin A Consultative Group by Dr. Paul Arthur. It was reviewed and approved by the IVACG Steering Committee.

immunizations is safe despite being associated with low rates of bulging of the anterior fontanel. However, as determined by the modified relative dose-response test (MRDR), this regimen produces only a small improvement in vitamin A status at six months of age. Furthermore, the resulting improvement in biochemical indices of vitamin A status does not persist up to nine months of age. This suggests that in populations with a high prevalence of breastfeeding, there is minimal benefit to supplementation of young infants with 25,000 IU of vitamin A at the time of their DPT/polio immunizations.

It has also now been shown conclusively that concurrent administration does not interfere with seroconversion to measles immunization at nine months or older. This follows the earlier report from one study in Indonesia which suggested that vitamin A administration may interfere with seroconversion following measles immunization if both measles vaccine and vitamin A are given to children who have high levels of passive immunity to measles at six months of age (Semba et al., 1995). However, this result was not replicated when measles vaccine was administered at nine months of age (the recommended age for measles immunization) in subsequent studies in Guinea-Bissau (Benn et al., 1997) and Bangladesh (de Francisco and Ahmed, 1996). The impact of supplementation on the uptake of the DPT and polio immunizations has also been evaluated. In a recent review, a joint IVACG/WHO Task Force concluded that vitamin A supplementation given at the time of DPT, polio, and measles immunizations, and concluded that vitamin A does not reduce the immune response to these vaccines (Halsey et al., 2000).

References

Arthur P, Kirkwood B, Ross D, Morris S, Gyapong J, Tomkins A, Addy H (1992). Letter: Impact of vitamin A supplementation on childhood morbidity in northern Ghana. Lancet; 339:361-362.

Barreto ML, Santos LMP, Assis AMO, et al. (1994). Effect of vitamin A supplementation on diarrhoea and acute lower respiratory infection in young children in Brazil. Lancet; 344:228-231.

Beaton GH, Martorell R, Aronson KJ (1993). Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. State of the Art Series Nutrition Policy Discussion Paper No.13: United Nations Administrative Committee on Coordination/Subcommittee on Nutrition.

Benn CS, Aaby P, Bale C, et al. (1997). Randomised trial of effect of vitamin A supplementation on antibody response to measles vaccine in Guinea Bissau, West Africa. Lancet; 350:101-105.

Biswas R, Biswas AB, Manna B, Bhattacharya SK, Dey R, Sarkar S (1994). Effect of vitamin A supplementation on diarrhoea and acute lower respiratory tract infection in children. Eur J Epidemiol; 10:57-61.

Conclusion

The benefits of vitamin A supplementation to children above six months of age have been clearly shown, and this has spurred vitamin A-deficiency control initiatives around the world. Young infant supplementation with 25,000 IU vitamin A is safe. The most frequently reported side effect, bulging of the anterior fontanel, is benign and transient, and currently there is no evidence of associated long-term neurological deficit. There also is no indication that supplementation at this time will reduce seroconversion to DPT and polio immunizations. However, supplementation with 25,000 IU of vitamin A at the time of each DPT/polio immunization does not produce a sustained improvement in vitamin A status beyond six months of age. To achieve this, it will be necessary to provide additional vitamin A (100,000 IU) at six months of age, and or increase the size and frequency of the dose, an issue that is currently under consideration.

de Francisco A, Chakraborty J, Chowdry HR, et al. (1993). Acute toxicity of vitamin A given with measles in infancy. Lancet; 342:526-527.

de Francisco A, and Ahmed F (1996). Measles vaccine failure not associated with vitamin A supplementation. Trans Roy Soc Trop Med Hyg; 90:441.

Fawzi WW, Chalmers TC, Herrera MG, Mosteller F (1993). Vitamin A supplementation and child mortality: a meta-analysis. JAMA; 269:989-903.

Glaziou PP and Mackerras DEM (1993). Vitamin A supplementation and infectious disease: a meta-analysis. BMJ; 306:366-370.

Halsey NA, Clements J, Sommer A, et al. (2000) Combining Vitamin A Distribution with EPI Contacts. Report of an IVACG Task Force, Washington, DC: International Life Sciences Institute.

Semba RD, Munasir Z, Beeler J, et al. (1995) A reduced seroconversion to measles in infants given vitamin A with measles vaccination. Lancet; 345:1330-1332.

Semba RD, Akib A, Beeler J, et al. (1997) Effect of vitamin A supplementation on measles vaccination in nine-month old infants. Public Health; 111:245-247.

Tonascia JA (1993). Meta-analysis of published community trials: impact of vitamin A on mortality. Proceedings of the Bellagio Meeting on vitamin A deficiency and childhood mortality. New York: Helen Keller International.

WHO (1993). Using immunisation contacts to combact vitamin A deficiency. Report of an informal consultation: WHO, Geneva, June 30-July 1, 1992. WHO/NT/EPI/93.1. WHO; Geneva.

WHO (1994). Using immunisation contacts as the gateway to eliminating vitamin A deficiency. A policy document. WHO/EPI/GEN/94.9. World Health Organisation, Geneva,.

WHO (1997). Joint WHO/UNICEF/IVACG Task Force: Vitamin A Supplementation: A guide to their use in the treaatment and prevention of vitamin A deficiency and xerophthalmia. 2nd ed.; WHO; Geneva.

WHO/CHD Immunisation-Linked Vitamin A Supplementation Multicentre Group (1998). Randomised trial to assess the benefits and safety of vitamin A supplementation linked to immunisations in early infancy. Lancet; 352:1257-63.

Photos courtesy of Laurie Lindsay Aomari

About IVACG

Established in 1975, the International Vitamin A Consultative Group guides international activities for reducing vitamin A deficiency in the world. IVACG concentrates its efforts on stimulating and disseminating new knowledge, translating that new knowledge to enable its practical application, and providing authoritative policy statements and recommendations that others can use to develop appropriate prevention and control programs.

IVACG Steering Committee

IVACG Secretariat Staff

The publication of this statement is made possible by support from Micronutrient Global Leadership, a project of the Office of Health and Nutrition, Bureau for Global Programs, Field Support and Research, U.S. Agency for International Development, under Cooperative Agreement Number HRN-A-00-98-00027-00.

August 2000

Printed in the United States of America

Additional copies of this and other IVACG publications are available free of charge to developing countries and for US$3.50 to developed countries. Copies can be ordered from the IVACG Secretariat:

IVACG Secretariat
ILSI Research Foundation
1126 Sixteenth Street, NW
Washington, DC 20036-4810
USA

Tel: 202-659-9024
Fax: 202-659-3617
E-mail: hni@ilsi.org
www.ilsi.org/ivacg.html

International Vitamin A Consultative Group ▲ IVACG

The ILSI Research Foundation's Human Nutrition Institute serves as the IVACG Secretariat.